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09/772,445	01/29/2001	Hynda K. Kleinman	2600-109	1045

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EXAMINER	
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ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
06/09/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	09/772,445	KLEINMAN ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *187-236* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 189,190,197,201,206,207,214,218,222,230,233 and 234.

Continuation of Disposition of Claims: Claims rejected are 187,188,191-196,198-200,202-205,208-213,215-217,219-221,223-229,231,232,235 and 236.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/30/10 has been entered.

Applicants amendments and arguments filed 3/30/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn. The previous 112 2nd and 112 1st new matter rejections have been overcome by the amendments.

Previously, applicant elected group 1 (claims 1-40,47-49,53-61,133-136) (11/5/04) and elected a species comprising amino acids LKKTET (2/24/05) for the would healing polypeptide. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Due to the addition of new claims an additional election of species requirement was sent 1/6/09.

Applicant's election of the following species:

Patient population: skin wound

Further agent: transforming growth factor beta

Further excipient: sterile water

in the reply filed on 2/5/09 is acknowledged.

In the instant case, each of the elected species were found in the prior art. In particular the peptide thymosin beta 4 comprises LKKTET (compare claim 188). Any art that was found in the course of searching for the elected species that reads on non-elected species is also cited herein. In accord with section 803.02 of the MPEP the Markush-type claims and the claims to the elected species are rejected and claims to the nonelected species are held withdrawn from consideration. In accord with section 803.02 of the MPEP the search is not extended unnecessarily to cover all species (such as all isoforms).

Claims 1-186 have been cancelled.

Claims 189-190,206-207 are to a species other than thymosin beta 4 (i.e. an LKKTET containing peptide), claims 197,201,214,218,230,233-234 are to a species of further agent other than transforming growth factor beta, claim 222 is to a patient population other than skin wound.

Claims 189-190,197,201,206-207,214,218,222,230,233,234 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/5/09.

Claims 187-188,191-196,198-200,202-205,208-213,215-217,219-221,223-229,231-232,235-236 are under consideration.

Priority

A section entitled 'priority' appeared in previous office action. Based on the claim amendments the section has been updated.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/094,690 (7/30/98), fails to provide adequate written description in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

In the instant case, Claims 187,191-196,198-200,202-204,208-213,215-217,219-221,223-224,226-229,231-232,235-236 refer to the amino acid sequence LKKTET or to isoforms.

Lack of Ipsis Verbis Support

Application No. 60/094,690 (7/30/98), is void of support for the amino acid sequence LKKTET or for isoforms.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

Although the above statement is with respect to new claim limitations, the analysis is similar in determining conditions for receiving the benefit of an earlier filing date.

Application No. 60/094,690 (7/30/98), does recite thymosin beta 4. However, the disclosure of thymosin beta 4 would not lead one to the sequence LKKTET or to isoforms. For at least these reasons, one would not conclude that Application No. 60/094,690 provides adequate support for Claims 187,191-196,198-200,202-204,208-213,215-217,219-221,223-224,226-229,231-232,235-236.

Claim Rejections - 35 USC § 112

These 112 rejections are new rejections.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 194,229 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 194 recites the limitation "said carrier" in claim 187. There is insufficient antecedent basis for this limitation in the claim. Claim 187 does not recite a carrier.

Claim 229 recites the limitation "said mammal" in claim 224. There is insufficient antecedent basis for this limitation in the claim. Claim 224 does not recite a mammal.

Although unclear, for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear, for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

Claim Rejections - 35 USC § 102

Claims were previously rejected under 102 based on the references cited herein. Since the claims have been amended the rejections have been updated.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 187-188,192-193,195-196,200,202-205,209-210,212-213,217,219-221,223-226,228,235-236 are rejected under 35 U.S.C. 102(b) as being anticipated by Turischev (Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' v45 (1996) pages 42-43; first cited 12/30/09) as evidenced by Mann (US 6,030,948).

It is noted that Turischev is in a non-English language. A translated version of the article has been provided and will be relied upon and referenced to herein (Turischev translation of Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' total of 7 pages including the cover page)

Turischev teach the effect of thymosin on the healing of flat skin wounds in rats (title). Turischev teach that Thymosin (5^{th} fraction) was used in the experiments (page 1 last paragraph).

Turischev teach that the composition was administered intraperitoneally or topically to rats with wounds (page 2). Turischev teach that there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3). Turischev does not recite the components of thymosin 5th fraction. Mann teach (column 4 lines 8-53) that thymosin fraction 5 contains thymosin beta4 (column 4 line 31) and thymosin alpha 1 (column 4 line 26). Mann is cited as a universal fact to reveal the components of thymosin fraction 5 and thus need not be prior art (MPEP 2124).

Since Turischev teach rats with skin wounds the patient population of claims 187,202,203 (i.e. skin damage),204,219,220 (i.e. epidermal),221,223 (skin damage),224,226,228 are met. Since Turischev teach that the composition was administered intraperitoneally or topically via a solution (page 2) the limitations of claims 192-193,195,196,209,210,212,213,235,236 are met. Turischev teach that Thymosin (5th fraction) was used in the experiments (page 1 last paragraph) and Mann states that such fraction contains thymosin beta 4 and thymosin alpha 1 (see applicants original claim 12 and admission on page 21 lines 4-5 of the reply dated 3/30/10, and see page 11 of specification of the current invention) the composition limitations of claims 187,188,200,204,205,217,224,225 are met.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since Turischev teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). It is noted that the claims refer to effective amounts. Since Turischev expressly states (page 3) 'this is evidence of a clear acceleration of the healing rates' and 'a dose of 0.8 ug accelerated wound healing' the amounts are effective.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd), for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear (see 112 2nd), for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

Response to Arguments 102 Turischev

Applicants argue (pages 19-21) that the effects of Turischev are unreliable and one would likely ignore the teachings completely.

Applicants argue that Turischev does not teach any role in wound repair in contrast to wound healing.

Applicants argue that the thymic fraction employed in Turischev contains different active peptides but it is not clear which is responsible for the activities.

Applicants argue that there is no indication that effects were the result of thymosin beta 4.

Applicant's arguments filed 3/30/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 19-21) that the effects of Turischev are unreliable and one would likely ignore the teachings completely, Section 2121 expressly states that prior art is

presumed to be enabled. Since the prior art teach the active steps the claim limitations are met. Further, Turischev expressly states (page 3) 'this is evidence of a clear acceleration of the healing rates' and 'a dose of 0.8 ug accelerated wound healing'. Further section 2131.05 states: The question whether a reference "teaches away" from the invention is inapplicable to an anticipation analysis.

Although Applicants argue that Turischev does not teach any role in wound repair in contrast to wound healing, it is noted that the instant specification does not provide any specific definition for wound repair or wound healing. In other words, although applicants try to differentiate between the two there is no basis for doing such. Further the dictionary (The Free online dictionary (entry for healing) http://www.thefreedictionary.com/healing accessed on 5/26/10 4 pages) expressly defines healing to be repair (page 1, heal 2nd definition). Applicants assertion is contradictory to the term definition.

Although Applicants argue that the thymic fraction employed in Turischev contains different active peptides but it is not clear which is responsible for the activities, it is noted that the instant claims recite that the composition 'comprises' certain components. In accord with section 2111.03 of the MPEP comprising is open-ended language. Thus other components are permissible. Further, it is noted that the claims are not drawn to methods of determining what is responsible for the activities. Since the prior art teach the active steps the claim limitations are met.

Although Applicants argue that there is no indication that effects were the result of thymosin beta 4, it is noted that the claims are not drawn to methods of determining effects. Since the prior art teach the active steps the claim limitations are met.

This 102e rejection using the Mann reference is based on a previous rejection. The rejection has been updated due to the claim amendments.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 187-188,192-193,195-196,200,202-205,209-210,212-213,217,219-220,223-226,228-229,235-236 are rejected under 35 U.S.C. 102(e) as being anticipated by Mann (US 6,030,948). It is noted that the 102(e) date for Mann is Dec. 19, 1997 based on MPEP section 706.02(f)(1) section III for a patent that is not from an international application and in which there is no international application in the continuity chain.

Mann teach a composition (claim 1, Tables 13-16) containing thymosin fraction 5. The thymosin fraction 5 includes both thymosin β4 (which comprises the sequence LKKTET) and thymosin α1 (which itself can augment the wound healing process – see page 11 of specification of the current invention thus meeting the limitation of claim 3 for example).

Claim 8 of Mann also teaches combinations of thymosin α1 and thymosin β4 thus meeting the composition limitations recited in claims 187-188,200.204-205,217,224-225 of the instant invention.

Mann teach a method of applying this composition to the scalp (claim 8). Prior to application to the scalp, an acid peel (i.e. chemical peel) solution is applied to the scalp and then removed. As such, the patient is in need of skin regeneration as recited in the instant claims. Further, there is a reasonable basis that the removal of an acid peel solution would result in the removal of an outer layer of the skin and result in abrasion/damage/lesions/wounds on the skin. Mann teach that the composition can be applied topically as a lotion or gel (column 3 lines 52-63), and teach a vehicle (Table 14 for example) and can be used for males or females (Tables 13-16). Thus the limitations of claims 187-188,192-193,195-196,200,202-205,209-210,212-213,217,219-220,223-226,228-229,235-236.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since Mann teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). It is noted that the claims refer to effective amounts. Since Mann teach specific amounts (Table 14) such amounts are deemed effective absent evidence to the contrary.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd), for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear (see 112 2nd), for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

Response to Arguments 102 Mann

Applicants argue (pages 12-19) that the reference does not meet the claim limitations particularly with respect to the patient population.

Applicants argue that the previously submitted declaration states that the prior art methods do not produce a wound.

Applicants argue that Mann does not teach wounding the skin and the treatments are not intended to do so.

Applicants argue that the action of the peel is to loosen and dissolve skin chemically.

Applicants argue that broken skin is skin that has an open defect that exposes internal structures or the bloodstream.

Applicants argue that the claims do not define the wound as the office implies.

Applicants argue that the amount of thymosin beta 4 as described by Mann is not enough to achieve the claims.

Applicants argue that the acid peel system includes physiological acids and nowhere refers to any wounds.

Applicant's arguments filed 3/30/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 12-19) that the reference does not meet the claim limitations particularly with respect to the patient population, in the instant case the claims recite promoting wound repair and regeneration in a subject in need of such treatment. Although not relied upon in the rejection, it is noted that TheFreeDictionary (The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages) teach that a wound involves the skin or another external surface being torn, pierced, cut, or otherwise broken (page 1). In the instant case, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. Applicants have admitted on the record (8/31/09 reply page 26 line 22) "it is commonly known in the art that chemical and acid peel treatments refer to causing the outer dead layers to peel away…'. As such, the acid peel of Mann would necessarily cause skin layers to peel away. Causing skin layers to be peeled away seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken'. In other words it is unclear how skin can be removed if it is not broken away from other skin. Further, since applicants admission shows that skin is peeled away during an acid peel one would recognize such skin as

in need of regeneration as is recited in the instant claims. It is noted that the applicants specification suggests a broad interpretation of the word 'wound'. In the instant case, claims 133-134,185-186 of the 8/31/09 claim set are evidence that the term 'wound' is to be broadly, as opposed to narrowly, interpreted. Thus the broadest reasonable interpretation of 'wound' is consistent with the broad disclosure of the specification and dictionary definitions (see MPEP section 2111).

Although Applicants argue that the previously submitted declaration states that the prior art methods do not produce a wound, such declaration was previously addressed and such arguments remain of record. Section 716.01(c) of the MPEP states:
'In assessing the probative value of an expert opinion, the examiner must consider the nature of the matter sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985), cert. denied, 475 U.S. 1017 (1986).' In the instant case, the expert is of the opinion that that any person skilled in the art would recognize that surface acting peels do not cause abrasion/damage/lesions/wounds on skin. However, specific facts or data or references to support such a conclusion are not convincingly set forth. It is noted that the declaration refers to Table 10 of Mann. Although the expert asserts and concludes that such composition would have certain properties, no experimental or documentary evidence has been provided. As quoted above section 716.01(c) of the MPEP states that the interest of the expert in the outcome is a factor to consider. In the instant case, Regenerx Corporate Presentation (retrieved from

http://www.regenerx.com/pdf/NCInvestorPresentation_v38.ppt on 4/13/09 34 pages) teach that (page 32) Jo-David Fine, the expert listed in the declaration, is an advisor for the company Regenerx whose founder (page 31-32) is one of the inventors of the instant invention. As such, there is a reasonable basis that the expert has an interest in the outcome. In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence fails to outweigh the evidence of record. Further, applicants have admitted on the record (8/31/09 reply page 26 line 22) "it is commonly known in the art that chemical and acid peel treatments refer to causing the outer dead layers to peel away…'. As such, the acid peel of Mann would necessarily cause skin layers to peel away. Causing skin layers to be peeled away seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken' (see definition of wound, The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages).

Although Applicants argue that Mann does not teach wounding the skin and the treatments are not intended to do so, it is noted that the claims recite 'regeneration in a subject in need of such'. Applicants have admitted on the record (8/31/09 reply page 26 line 22) "it is commonly known in the art that chemical and acid peel treatments refer to causing the outer dead layers to peel away…'. As such, the acid peel of Mann would necessarily cause skin layers to peel away. Causing skin layers to be peeled away seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken' (see definition of wound, The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages).

Although Applicants argue that the action of the peel is to loosen and dissolve skin chemically, applicants have clearly stated on the record: (8/31/09 reply page 26 line 22) "it is

commonly known in the art that chemical and acid peel treatments refer to causing the outer dead layers to peel away…'. As such, the acid peel of Mann would necessarily cause skin layers to peel away. Causing skin layers to be peeled away seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken' (see definition of wound, The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages).

Although Applicants argue that broken skin is skin that has an open defect that exposes internal structures or the bloodstream, it is first noted that the instant claims do not recite broken skin. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., broken skin) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, such proposed definition as asserted by applicant is not found in the specification as originally filed nor has applicant cited such definition as being from the art.

Although Applicants argue that the claims do not define the wound as the office implies, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. . Applicants have admitted on the record (8/31/09 reply page 26 line 22) "it is commonly known in the art that chemical and acid peel treatments refer to causing the outer dead layers to peel away…'. As such, the acid peel of Mann would necessarily cause skin layers to peel away. Causing skin layers to be peeled away seems to be reasonably within the realm of 'being

torn,pierced,cut, or otherwise broken' (see definition of wound, The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages).

Although Applicants argue that the amount of thymosin beta 4 as described by Mann is not enough to achieve the claims, such statement amounts to an assertion and not factual evidence. Section 2145 of the MPEP states the arguments of counsel cannot take the place of evidence in the record. Mann teach specific amounts (Table 14), such amounts are deemed effective absent evidence to the contrary. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Although Applicants argue that the acid peel system includes physiological acids and nowhere refers to any wounds, Applicants have admitted on the record (8/31/09 reply page 26 line 22) "it is commonly known in the art that chemical and acid peel treatments refer to causing the outer dead layers to peel away…'. As such, the acid peel of Mann would necessarily cause skin layers to peel away. Causing skin layers to be peeled away seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken' (see definition of wound, The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages).

Claim Rejections - 35 USC § 103

The 103 rejection based on Turischev is a new rejection; other 103 rejections are based on previous rejections.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 187-188,191-196,198-200,202-205,208-213,215-217,219-221,223-229,231-232,235-236 are rejected under 35 U.S.C. 103(a) as being unpatentable over Turischev (Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats'

v45 (1996) pages 42-43; first cited 12/30/09) and Mann (US 6,030,948) and Puolakkainen et al (Journal of Surgical Research v58 1995 pages 321-329 first cited 4/29/09).

It is noted that Turischev is in a non-English language. A translated version of the article has been provided and will be relied upon and referenced to herein (Turischev translation of Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' total of 7 pages including the cover page)

Turischev teach the effect of thymosin on the healing of flat skin wounds in rats (title). Turischev teach that Thymosin (5^{th} fraction) was used in the experiments (page 1 last paragraph). Turischev teach that the composition was administered intraperitoneally or topically to rats with wounds (page 2). Turischev teach that there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3). Turischev does not recite the components of thymosin 5^{th} fraction. Mann teach (column 4 lines 8-53) that thymosin fraction 5 contains thymosin beta4 (column 4 line 31) and thymosin alpha 1 (column 4 line 26). Mann is cited as a universal fact to reveal the components of thymosin fraction 5 and thus need not be prior art (MPEP 2124).

Turischev does not expressly teach transforming growth factor beta as recited in claims 198-199,215-216,231-232. Turischev does not expressly teach recombinant or synthetic polypeptides as in claims 191 and 208. Turischev does not expressly teach sterile water as a carrier as recited in claims 194,211. Turischev does not expressly teach contacting as in claims 227,229.

Turischev teach the effect of thymosin on the healing of flat skin wounds in rats (title). Turischev teach that Thymosin (5th fraction) was used in the experiments (page 1 last paragraph). Turischev teach that the composition was administered intraperitoneally or topically to rats with wounds (page 2). Turischev teach that there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3). Turischev does not recite the components of thymosin 5th fraction. Mann teach (column 4 lines 8-53) that thymosin fraction 5 contains thymosin beta4 (column 4 line 31) and thymosin alpha 1 (column 4 line 26). Mann is cited as a universal fact to reveal the components of thymosin fraction 5 and thus need not be prior art (MPEP 2124). Since Turischev teach rats with skin wounds the patient population of claims 187,202,203 (i.e. skin damage),204,219,220 (i.e. epidermal),221,223 (skin damage),224,226,228 are met. Since Turischev teach that the composition was administered intraperitoneally or topically via a solution (page 2) the limitations of claims 192-193,195,196,209,210,212,213,235,236 are met. Turischev teach that Thymosin (5th fraction) was used in the experiments (page 1 last paragraph) and Mann states that such fraction contains thymosin beta 4 and thymosin alpha 1 (see applicants original claim 12 and admission on page 21 lines 4-5 of the reply dated 3/30/10, and see page 11 of specification of the current invention) the composition limitations of claims 187,188,200,204,205,217,224,225 are met.

Turischev teach that the composition was administered via a solution (page 2). One would recognize water as a common component of a solution. Since the experiments are carried out on live mammals one would want to ensure that there is no unnecessary contamination and thus one would be motivated to use sterile water. Since Turischev expressly teach positive results (there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound

healing (page 3)) one would be motivated to carry out the methods of Turischev. Since water is a common component of a solution one would be motivated to use such component thus meeting the limitation recited in claims 194,211. In other words, in order to use the TB4 for skin wounds one would be motivated to prepare the TB4 with an appropriate excipient such as water and an appropriate form such as a lotion for administration to the skin. Further, since Turischev teach positive results (there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3)) one would be motivated to perform further experiments, for example ex vivo experiments and experiments in humans thus meeting the limitations as recited in claims 227,229. One would have a reasonable expectation of success since Turischev expressly teach positive results (there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3)).

Like Turischev, Puolakkainen also teach experiments that test methods of wound healing in rats (abstract). Puolakkainen recognize what is well-known in the art, that TGF-beta is known to enhance wound healing (title, page 325 discussion). In fact, Puolakkainen teach that TGF-beta significantly enhanced wound healing (abstract). One would be motivated to use the teachings of Puolakkainen along with Turischev since the references are drawn to methods of wound healing. The ides of combining them logically flows from their having been individually aught in the art. As such, one would be motivated to administer both thymosin beta 4, TGF-beta thus meeting the limitations as recited in claims 198-199,215-216,231-232. Further, Puolakkainen recognizes (page 322 section preparation of the TGF-beta) using recombinant forms of the proteins. One would be motivated to also use recombinant forms of the other proteins thus meeting the limitations recited in claims 191 and 208.

In the instant case, the claimed elements (thymosin beta 4, TGF-beta) were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Taken together the references meet the limitations of the instant claims. One would have a reasonable expectation of success since both references teach agents for wound healing.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since Turischev teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). It is noted that the claims refer to effective amounts. Since Turischev expressly states (page 3) 'this is evidence of a clear acceleration of the healing rates' and 'a dose of 0.8 ug accelerated wound healing' the amounts are effective.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd), for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear (see 112 2nd), for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

Claims 187-188,191-196,200,202-205,208-213,217,219-221,223-229,235-236 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malinda et al (Faseb Journal 1997 cited in IDS 5/25/01) and Baumann et al 1997 (from 'Thymic peptides in preclinical and clinical medicine: an update:proceedings of the 2nd international thymus symposium' editor HR Maurer, pages 13-17) and Biotech Patent News (Dec 1 1997 1 page).

Malinda teach that Thymosin beta 4 (TB4) acts as a chemoattractant for endothelial cells (abstract). Malinda teach that in vitro wound closure is more rapid in the presence of TB4 (page 477). Malinda teach that cell migration is enhanced by TB4 (page 478). Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of wound healing (page 480). Malinda teach that others report that TB4 could play a major role in would healing (page 480).

Malinda does not expressly teach administration of TB4 to patients in need of wound repair.

Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of wound healing (page 480). Malinda teach that others report that

TB4 could play a major role in would healing (page 480). Malinda recognizes the use of in vivo experiments (abstract). Since Malinda teach positive results for the in vitro studies (see wound closure model page 477) one would be motivated to use the method in vivo.

Further, Baumann (Table II page 21) also teach that TB4 leads to an increase in wound healing in vitro.

Further, Biotech Patent News teach that investigators will use thymosin beta 4 (last paragraph) in a wound healing study.

Taken together, the prior art clearly recognizes the use of TB4 for wound healing. Although the references do not expressly teach in a single embodiment the use for patients in need thereof one would be motivated to use TB4 in patients based on the promising in vitro results. One would have a reasonable expectation of success based on the in vitro results reported in the prior art.

Since Biotech patent news teach the use in wound healing studies one would be motivated to use TB4 specifically for those with wounds. Since Malinda teach the use of a scratch wound closure assay (page 475) one would be motivated to use TB4 in vivo for skin wounds. In order to use the TB4 for skin wounds one would be motivated to prepare the TB4 with an appropriate excipient such as water (in particular sterile water to prevent contamination) and an appropriate form such as a lotion for administration to the skin. Since in vitro models are used as a precursor to use in humans one would be motivated to use the methods on humans and apply TB4 to skin cells including epithelial cells (see page 474 of Malinda) based on the promising in vitro results. Although Malinda does not recite the source of the protein one would recognize that recombinant or synthetic production is a well known method in the art for

production of peptides. Thus taken together the references obviate the use of a specific agent (thymosin beta 4) which reads on the polypeptide as recited in the instant claims; the references motivate a specific use (wound healing) which motivates specific excipients, forms, and locations of administration as recited in the instant claims.

Further, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g.doses), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2144.05). Thus, taken together the limitations of claims 187-188,191-196,200,202-205,208-213,217,219-221,223-229,235-236 rendered obvious based on the prior art.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since Malinda teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01).

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd), for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear (see 112 2nd), for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

Claims 187-188,191-196,198-200,202-205,208-213,215-217,219-221,223-229,231-232,235-236 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malinda et al (Faseb Journal 1997 cited in IDS 5/25/01) and Baumann et al 1997 (from 'Thymic peptides in preclinical and clinical medicine: an update:proceedings of the 2nd international thymus symposium' editor HR Maurer, pages 13-17) and Biotech Patent News (Dec 1 1997 1 page) and Puolakkainen et al (Journal of Surgical Research v58 1995 pages 321-329).

As discussed above, Malinda, Baumann, and Biotech Patent News teach the use of TB4 for wound healing and render obvious claims 187-188,191-196,200,202-205,208-213,217,219-221,223-229,235-236.

However, the references do not expressly teach in a single embodiment the use of a further agent or the use of TGF-beta as in claims 198-199,215-216,231-232.

Puolakkainen recognize what is well-known in the art, that TGF-beta is known to enhance wound healing (title, page 325 discussion). Puolakkainen also recognize the optimization of the administration mode and dose and teach toward topical administration (abstract and throughout). One would be motivated to use the teachings of Puolakkainen along with the other references since the references are drawn to methods of wound healing.

In the instant case, the claimed elements (thymosin beta 4, TGF-beta) were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Taken together the references meet the limitations of the instant claims. One would have a reasonable expectation of success since both references teach agents for wound healing. Taken together the references render obvious claims 187-188,191-196,198-200,202-205,208-213,215-217,219-221,223-229,231-232,235-236.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since Malinda teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01).

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd), for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear (see 112 2nd), for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

Claims 187-188,191-196,200,202-205,208-213,217,219-221,223-229,235-236 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mann (US 6,030,948).

As discussed above (see 102 e rejection), Mann teach methods of administering a composition comprising thymosin β4.

Mann does not expressly teach the use of a recombinant or synthetic TB4 as in claims 191,208; the ex vivo use as in claim 227; the use of sterile water as in claims 194,211.

Mann does expressly teach the use of thymosin beta 4 (claim 8). Since recombinant expression and purification of proteins is well-known in the art one of skill in the art would have been motivated to substitute the thymus purified peptide as taught by Mann with a recombinant or synthetic peptide while maintaining an expectation of predictable results since the primary sequence of the protein is retained. Thus Mann obviates claims 191,208 of the instant invention.

Mann expressly teach the use of a vehicle (Tables 14-16) for the compositions. Since maintaining a pure, uncontaminated product is a goal one would be motivated to use sterile water as a specific vehicle while maintaining an expectation of predictable results since the same active ingredients are used. Thus Mann obviates claim 194,211 of the instant invention

Mann recognizes the use of in vitro experiments (Table 1). It would be obvious to one of skill in the art to determine if similar results could be obtained *in vitro* so that experimental results could be achieved in a more cost effective manner in a laboratory setting instead of requiring human subjects. Thus Mann obviates claim 227 of the instant invention.

Mann teach a composition (claim 1, Tables 13-16) containing thymosin fraction 5. The thymosin fraction 5 includes both thymosin β4 (which comprises the sequence LKKTET) and thymosin α1 (which itself can augment the wound healing process – see page 11 of specification of the current invention thus meeting the limitation of claim 3 for example).

Claim 8 of Mann also teaches combinations of thymosin α1 and thymosin β4 thus meeting the composition limitations recited in claims 187-188,200.204-205,217,224-225 of the instant invention.

Mann teach a method of applying this composition to the scalp (claim 8). Prior to application to the scalp, an acid peel (i.e. chemical peel) solution is applied to the scalp and then removed. As such, the patient is in need of skin regeneration as recited in the instant claims. Further, there is a reasonable basis that the removal of an acid peel solution would result in the removal of an outer layer of the skin and result in abrasion/damage/lesions/wounds on the skin. Mann teach that the composition can be applied topically as a lotion or gel (column 3 lines 52-63), and teach a vehicle (Table 14 for example) and can be used for males or females (Tables 13-

16). Thus the limitations of claims 187-188,192-193,195-196,200,202-205,209-210,212-213,217,219-220,223-226,228-229,235-236.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since Mann teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). It is noted that the claims refer to effective amounts. Since Mann teach specific amounts (Table 14) such amounts are deemed effective absent evidence to the contrary.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd), for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear (see 112 2nd), for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Response to Arguments 103

Applicants argue (pages 21-24) that Mann does not teach or even suggest treating a wound it cannot render the claims obvious.

Applicants argue that Mann does not suggest that the compositions contained the activity recited in the claims.

Applicants argue that in vitro models of Malinda in no way correlate with in vivo wound healing.

Applicants argue there is no reasonable expectation of success based on Baumann and Biotech Patent News or Puolakkainen and that that Biotech News is not peer-reviewed

Applicants argue that Baumann teach wound closure not wound repair.

Applicant's arguments filed 3/30/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 21-24) that Mann does not teach or even suggest treating a wound it cannot render the claims obvious as discussed above applicants have admitted on the record (8/31/09 reply page 26 line 22) "it is commonly known in the art that chemical and acid peel treatments refer to causing the outer dead layers to peel away…'. As such, the acid peel of Mann would necessarily cause skin layers to peel away. Causing skin layers to be peeled away seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken' (see definition of wound, The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages).

Although Applicants argue that Mann does not suggest that the compositions contained the activity recited in the claims, Mann expressly teach thymosin beta four as a component (claim 8). Thymosin beta four is expressly recited in claim 188. Since Mann teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01).

Although Applicants argue that in vitro models of Malinda in no way correlate with in vivo wound healing, such statement amount to an assertion and not factual evidence. Section 2145 of the MPEP states the arguments of counsel cannot take the place of evidence in the record. Prior art is presumed to be enabled (MPEP section 2121). Further, obviousness does not require absolute predictability (MPEP section 2143.02). Malinda expressly teach that in vitro wound closure is more rapid in the presence of TB4 (page 477), thus one would have a reasonable expectation of success.

Although Applicants argue there is no reasonable expectation of success based on Baumann and Biotech Patent News or Puolakkainen and that that Biotech News is not peer-reviewed, none of the references appear to discourage or disparage wound treatments. Baumann (Table II page 21) teach that TB4 leads to an increase in wound healing in vitro. Further, Biotech Patent News teach that investigators will use thymosin beta 4 (last paragraph) in a wound healing study. Puolakkainen recognize what is well-known in the art, that TGF-beta is known to enhance wound healing (title, page 325 discussion). Obviousness does not require absolute predictability (MPEP section 2143.02). With regards to Biotech News not being peer-reviewed such statement is an assertion. Further, there is no basis to exclude prior art on the basis of whether or not it is peer reviewed.

Although Applicants argue that Baumann teach wound closure not wound repair, it is noted that the instant specification does not provide any specific definition for wound repair or wound healing. In other words, although applicants try to differentiate between the two there is no basis for doing such. Further the dictionary (The Free online dictionary (entry for healing) http://www.thefreedictionary.com/healing accessed on 5/26/10 4 pages) expressly defines healing to be repair (page 1, heal 2nd definition). Applicants assertion is contradictory to the term definition. Further, one would recognize wound closure as part of the wound repair process.

Double Patenting

The double patenting rejections below are based on rejections from the previous office action. Since the claims have been updated the rejections have been updated to correspond to the instant claims.

The terminal disclaimer filed on 9/17/08 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 7,268,118 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on 9/17/08 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on 11/284,430 has been reviewed and is accepted. The terminal disclaimer has been recorded.

It is noted that 10/714,405 has been abandoned.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection

is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 187-188,191-193,195-196,198-200,202-205,208-210,212-213,215-217,219-220,223-225,231-232,235-236 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 48-73 of copending Application No. 11/284,408 (‘408). Although the conflicting claims are not identical, they are not patentably distinct from each other because the ‘408 application teaches methods of administering compositions to skin comprising thymosin beta four (for example, claim 48), transforming growth factor (claim 53), and a vehicle (claim 48) for topical treatment (for example, claim 52) in the form of a lotion (claim 72). ‘408 teach the administration to improve skin appearance and is applied to thinning skin (claim 53,70) thus one would be motivated to administer to those of the instant claims. Taken together, the limitations of claims 187-188,191-193,195-196,198-200,202-205,208-210,212-213,215-217,219-220,223-225,231-232,235-236 are met.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since '408 teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). It is noted that the claims refer to effective amounts. Since '408 expressly teach amounts (claim 48-49) and methods for improving the appearance of the skin (claim 53) the amounts are effective.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd), for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear (see 112 2nd), for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 187-188,191-193,195-196,198,200,202-205,208-210,212-213,215,217,219-220,223-225,231,235-236 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-23,26 of copending Application No. 11/917,869 ('869). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '869 application teaches methods of administering

compositions to the skin comprising thymosin beta four isoform or LKKTET (for example, claim 13,21), and a stimulating agent (claim 13), and a catteri (claim 17), and teach the composition as a lotion (claim 20), and teach specific doses (claim 23). The method is for treating tissue and injured or damaged skin thus one would be motivated to treat the patients as in the instant claims. Taken together, the limitations of claims 187-188,191-193,195-196,198,200,202-205,208-210,212-213,215,217,219-220,223-225,231,235-236 are met.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since '869 teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). It is noted that the claims refer to effective amounts. Since '869 expressly teach amounts (claim 23) and methods for treating (claim 13) the amounts are effective.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd), for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear (see 112 2nd), for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 187-188,191-193,195-196,200,202-205,208-210,212-213,219-220,223-225,235-236 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-32 of copending Application No. 11/715,997 ('997). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '997 application teaches methods of administering compositions to the skin comprising thymosin beta four or LKKTET (for example, claim 21), and specific doses (claim 27), and as a lotion (claim 22), and with a carrier (claim 23). The method is for treating tissue and injured or damaged skin thus one would be motivated to treat the patients as in the instant claims. Taken together, the limitations of claims 187-188,191-193,195-196,200,202-205,208-210,212-213,219-220,223-225,235-236 are met.

It is noted that certain claims recite properties – actin-sequestering activity, stimulates epithelial migration, etc. Since '997 teach the elected agent (i.e. thymosin beta 4) which is recited in the claims (claim 188 for example) the claim limitations are met (see also MPEP 2112.01). It is noted that the claims refer to effective amounts. Since '997 expressly teach amounts (claim 28) and methods for treating (claim 21) the amounts are effective.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting regeneration (claim 187) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd), for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear (see 112 2nd), for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 12/444,331 ('331). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '331 application teaches methods of administering compositions to the skin comprising thymosin beta four or LKKTET (for example, claim 1), and specific doses (claim 7), and lotions as a form (claim 11).The method is for treating tissue and injured or damaged skin thus one would be motivated to treat the patients as in the instant claims. Taken together, the limitations of claims 187-188,191-193,195-196,200,202-205,208-210,212-213,219-220,223-225,235-236 are met.

Although unclear (see 112 2nd), for purposes of examination claim 194 has been interpreted as referring to the carrier of claim 193. Although unclear (see 112 2nd), for purposes of examination claim 229 has been interpreted as referring to the mammal of claim 228.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 11/715,997 and 12/444,331; discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Response to Arguments Double Patenting

Applicants request (page 24) that the rejections be held in abeyance.

Applicant's arguments filed 3/30/10 have been fully considered but they are not persuasive.

Although Applicants request (page 24) that the rejections be held in abeyance, such request does not overcome the rejection. The instant claims are not allowable.

Prior art of record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Bilton (WO 84/02274) - Bilton teach compositions for wound healing (title) including those that include thymus concentrate (claim 1, example 1).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654